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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,725	05/26/2005	Daniel Christopher Brookings	Cell-0288	1007
23377 7590 12/03/2007 WOODCOCK WASHBURN LLP CIRA CENTRE, 12TH FLOOR 2929 ARCH STREET PHILADELPHIA, PA 19104-2891			EXAMINER O DELL, DAVID K	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/518,725	Applicant(s) BROOKINGS ET AL.	
	Examiner David K. O'Dell	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>19 September 2005</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. This application is a 371 of PCT/GB03/02667 filed 06/20/2003, which claims priority to Great Britain application 0214268.5 filed 06/20/2002.

Claims 1-31 are pending.

Response to Restriction/Election

2. Applicant's election of group I, and the species (the compound of Example 170) in the reply filed on November 9, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)). This requirement is made FINAL. This application contains claims drawn to a nonelected invention. A complete reply to this action must include a cancellation of nonelected claims or other appropriate action.

Under examination:

Group I, Claims 1-30 drawn to compounds and compositions reading on Formula 1 claim 1, Ar is phenyl, A is carbon with a double bond to the adjacent carbon, Y is a carbon, X is S, drawn to phenyl-amino-thienopyridinones. If this group is elected, a further election of a single disclosed species is also required. Further restriction based on the election may be made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites a "linker atom or group", however the identity of a linker atom or group is not defined. Claim 1 also recites several moieties that are not clearly defined by the

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specification including Alk1, Cy1 and "optional substituent". These groups are defined with exemplary language, as in Alk1:

"when Alk1 is present in compounds of formula (1) as an optionally substituted aliphatic chain it may be an optionally substituted C1-10aliphatic chain. Particular examples include optionally substituted straight or branched chain C1-6alkylene, C2-6alkenylene, or C2-6alkynylene chains."

The term "optionally substituted" is indefinite. Unless one knows what a substituent is, a determination of what these compounds are cannot be made. The specification does not fully elaborate the identity of these substituents. This rejection is not being made for breadth, which will be discussed at length in this action at 4. See MPEP 2173.05(d), for the use of exemplary language.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-28, 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds it does not reasonably provide enablement for the scope of compounds bearing the extensive list of substituents. The compounds that are enabled are as follows:

Y (which can only be a carbon atom due the restriction requirement) should be substituted with a carboxamide, namely carboxamides of the following formula, SO_2NH , $\text{CO}_2\text{-alkyl}$, CO_2H , COR (where R is morpholine, pyrrolidine, piperazine, piperidine,), C(=NH)NH_2 , C(=S)NH_2 , CN ,

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C=ONRaRp where Ra is alkyl or H, Rp is H, alkyl piperidine, pyrrolidine, alkanol, alkylamino, alkyl imidazole, or alkyl piperazine; R^b of A should be H, Ra on the ring should be H, R should be H, (Alk1)_n should be limited to (CH₂)_n, where n is 0 or 1, L should be limited to a bond, Cy1 should be a phenyl, pyridine, indole, thiophene, THP, or a cyclopropyl, the phenyls both Ar and the phenyl of Cy1 may be substituted with halogen, alkyl, sulfonamide, hydroxy, alkoxy, alkanol, trifluoromethyl, O-CF₃, OTBDMS, vinyl, alkyl-pyrrolidine, S(O)_nR (n is 0 1 or 2, R is alkyl), amino, or nitro. Please note the instantly claimed compounds cannot form N-oxides.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the following:

- (A) *The breadth of the claims;*
- (B) *The nature of the invention;*
- (C) *The state of the prior art;*
- (D) *The level of one of ordinary skill;*
- (E) *The level of predictability in the art;*
- (F) *The amount of direction provided by the inventor;*
- (G) *The existence of working examples; and*
- (H) **The quantity of experimentation needed to make or use the invention**

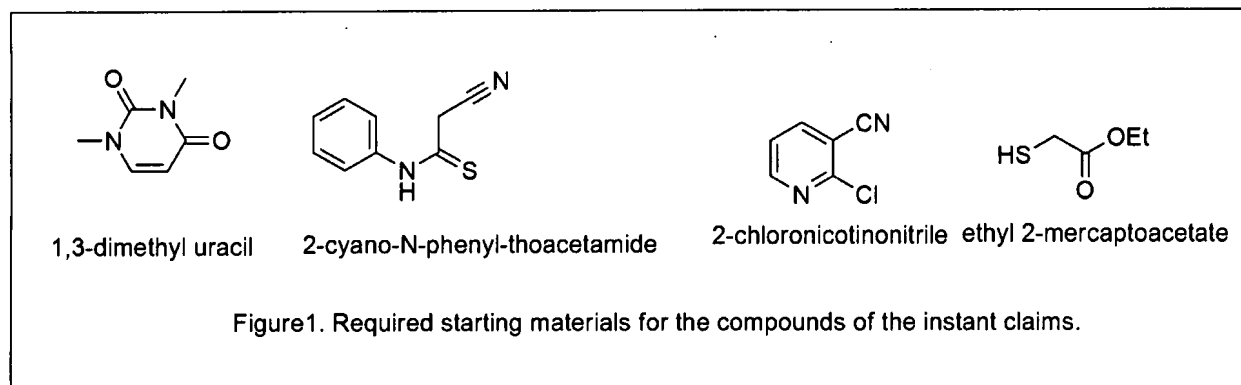
In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) The breadth of the claims: The claims are very broad encompassing all heterocycles, carbocycles and all other groups "optional substituents" bearing multiple "optional substituents"

(B) The nature of the invention: This is a chemical invention requiring the synthesis of compounds and such compounds should have activity at p38. **(D) The level of one of ordinary**

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skill: One of ordinary skill is a practicing organic/medicinal chemist. **(C) The state of the prior art:** **(E) The level of predictability in the art:** **(F) The amount of direction provided by the inventor,** **(G) The existence of working examples, and (H) The quantity of experimentation needed to make or use the invention:** Each one of the factors (C, E-H) will be discussed in light of the scientific literature when such a factor is being directly pointed to a large capital letter referring to the aforementioned Wands factor will be placed directly after such a remark or explication. The examiner will first consider the Markush structure I of claim 1, and discuss the limitations inherent to the chemistry required to prepare the compounds. The examples given for the construction of the ring system are the reaction of 2-chloro-3-cyanopyridine with 2-mercaptoethylacetate and the reaction of 2-cyano-N-phenyl-thioacetamide with uracil. These key materials are shown in Figure 1.



Where can one purchase the vast array 2-chloro-3-cyanopyridine or uracils, needed for the scope of the claimed substituents on Ra and Rb? The chemistry used to construct the compounds is not applicable to the scope claimed and currently no methods exist for the scope claimed. The limitations of synthetic chemistry is readily apparent as stated in the preface to a recent treatise:

“Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research

chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) [preface].....even structurally simple compounds often turn out not to be so easy to make as initially thought. [pg. 2]..... As illustrated by the examples discussed below, a good retrosynthesis requires much synthetic experience, a broad knowledge of chemical reactivity, and the ability to rapidly recognize synthetically accessible substructures [pg. 3]..... As will be shown throughout this book, the outcome of organic reactions is highly dependent on all structural features of a given starting material, and unexpected products may readily be formed. [8].....Even the most experienced chemist will not be able to foresee all potential pitfalls of a synthesis, specially so if multifunctional, structurally complex intermediates must be prepared.

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The close proximity or conformational fixation of functional groups in a large molecule can alter their reactivity to such an extent that even simple chemical transformations can no longer be performed. Small structural variations of polyfunctional substrates might, therefore, bring about an unforeseeable change in reactivity [pg. 9].....”

Dorwald F. A. *Side Reactions in Organic Synthesis*; 2005, Wiley:

VCH, Weinheim pg. IX of Preface pg. 1-15. (E)

The chemistry used to install the bromine on the 3-position of the thiophene ring (the Sandmeyer reaction), would react with the claimed substituents to give other groups, see: “Isopentyl Nitrite” Encyclopedia of Reagents for Organic Synthesis online “<http://www.mrw.interscience.wiley.com/eros/articles/ri074/sect0-fs.html> “ November 27, 2007.

Many of the compounds currently under the Markush claim could not exist but would self-polymerize instantaneously if prepared as stated by Dorwald *ibid.* pg. 41 “It goes without saying that a compound will decompose or oligomerize if it contains functional groups which can react with each other. Because intramolecular reactions often proceed at much higher rates than their intermolecular variants, functional group incompatibilities may arise unexpectedly, involving groups which would not react intermolecularly...” (C & E)

As per MPEP:

A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In *re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

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According to the U.S. Court of Customs and Patent Appeals in *In re Argoudelis, De Boer, Eble, and Herr* 168 USPQ 99 at 101, "[o]rdinarily no problem in this regard arises since the method of preparing almost all starting materials can be set forth in writing if the materials are not already known and available to the workers in the art, and when this is done the specification is enabling to the public". *In re Argoudelis, De Boer, Eble, and Herr* 168 USPQ 99 at 104, "it is essential that there be no question that, *at the time an application for patent is filed*, (emphasis in original) the invention claimed therein is fully capable of being reduced to practice (i.e., that no technological problems, the resolution of which would require more than ordinary skill and reasonable time, remain in order to obtain an operative, useful embodiment)." That is not the situation here. Rather we find very little direction as to how the many required starting materials with these vast substituents are to be obtained. Where may the directions to prepare or buy them be found? (F)

In re Howarth, 210 USPQ 689, (claimed derivatives of clavulanic acid not enabled by specification lacking information of how prepare the clavulanic acid or directions to reference materials containing such information), *Ex parte Schwarze* 151 USPQ 426 (where starting material is not known to art as of date of filing application, there must be included a description of preparation thereof to enable one skilled in this art to carry out applicant's invention), *Ex parte Moersch* 104 USPQ 122 (claims to process for the production of (1)-yl-p-nitrophenyl-2-dichloracetamido-propane-1,3-diol not enabled because of failure to describe source or method of obtaining starting compound; although starting compound is identified by means of appropriate name and by structural formula).

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While these chemical limitations are significant, perhaps more significantly are the limitations of activity at p38. What are the important structural features for the claimed utility? Unfortunately the specification gives no data for the instantly claimed compounds. **(H)** The medicinal chemistry of p38 is relatively well-developed and many limitations are well known in the art. It is sensitive to structural changes that may be relatively minor in the chemical sense see, Michelotti et. al. "Two classes of p38a MAP kinase inhibitors having a common diphenylether core but exhibiting divergent binding modes" *Bioorganic & Medicinal Chemistry Letters* **2005**, *15*, 5274–5279.

"In compounds of Series 2, addition of a 4-fluoro group (compound 2a) (Fig. 2) to the diphenylether results in a 2- to 3-fold increase in potency, while substituents in the 2 and 3 positions appear to be unfavorable. Removal of the phenol hydroxyl of compound 2c results in a significant loss in activity (compound 2f), suggesting that this substituent plays an important role in binding. **Modification of the sulfamide linker of compound 2c to a sulfonamide linker (compound 2h) results in a complete loss of measurable activity.**"

Sadly in the instant case, the public has been given no details of regarding the choice of substituents required for activity. We have been given no information in regard to the molecular determinants of receptor affinity for the compounds of the instant case. **(F & G)** In this case the prepared compounds bear a structural resemblance to one another, yet the claims are not commensurate in scope. The factors outlined in *In Re Wands* mentioned above apply here, and in particular As per the MPEP 2164.01 (a): "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." It is very clear that one could not

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make/use this very broad invention that has only four working examples in this unpredictable art without undue experimentation. (C, E, F, G, H).

5. Claims 1-28, 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates and hydrates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims.

c) There is no working example of any hydrate or solvate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the

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postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

g) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate.

f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169

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USPQ 367, *In re Fisher*, 166 USPQ 18. h) The breadth of the claims includes all of the thousands of compounds of formula I as well as the presently unknown list of solvents embraced by the term "solvate".

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No.

10/524,199. Although the conflicting claims are not identical, they are not patentably distinct from each other because many of the instantly claimed species are embraced by the Markush structure of the '199 application and vice versa.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/561,050. Although the conflicting claims are not identical, they are not patentably distinct from each other because many of the instantly claimed species are embraced by the Markush structure of the '050 application and vice versa.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 1-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/561,052. Although the conflicting claims are not identical, they are not patentably distinct from each other because many of the instantly claimed species are embraced by the Markush structure of the '052 application and vice versa.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/576,731. Although the conflicting claims are not identical, they are not patentably distinct

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from each other because many of the instantly claimed species are position isomers of the Markush structure of the '731 case and vice versa.

Positional isomers, having the same radical on different positions of the molecule, are *prima facie* obvious, and require no secondary teaching. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these position isomers based on the expectation that such close analogues would have similar properties and upon the routine nature of such position isomer experimentation in the art of medicinal chemistry. It would be routine for the chemist to vary the point of attachment in order to increase potency and to establish better patent protection for her compounds. *In re JONES* 74 USPQ 152 (4-methyl naphthyl-1-acetic acid and 2-methyl naphthyl-1-acetic acid obvious over a reference teaching 1-methyl naphthyl-2-acetic acid), quoted with approval by *Ex parte MOWRY AND SEYMOUR* 91 USPQ 219, *Ex parte Ulliyot* 103 USPQ 185 (4-hydroxy-1-oxo-1,2,3,4-tetrahydroisoquinoline obvious over a reference teaching 4-hydroxy-2-oxo-1,2,3,4-tetrahydroquinoline), "[p]osition isomers are recognized by chemists as similar materials", *Ex parte BIEL* 124 USPQ 109 (N-ethyl-3-piperidyl diphenylacetate obvious over a reference teaching N-alkyl-4-piperidyl diphenylacetate), "[appellant's arguments] do not, in any way, obviate the plain fact that appellant's DACTIL is an isomer of McElvain et al.'s compound. This close relationship places a burden on appellant to show some unobvious or unexpected beneficial properties in his compound in order to establish patentability", *Ex parte Henkel* 130 USPQ 474, (1-phenyl-3-methyl-4-hydroxypyrazole obvious over reference teaching 3-phenyl-5-methyl-4-hydroxypyrazole), "appellants have made no comparative showing here establishing the distinguishing characteristics they allege which we might consider as evidence that the claimed

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compounds are unobvious. It is clear from *In re Henze*, supra, and the authorities it cites, that at least this much is necessary to establish patentability in adjacent homologs and **position isomers** (emphasis added)".

In re Surrey 138 USPQ 67, (2,6-dimethylphenyl-N-(3-dimethylaminopropyl) carbamate obvious over a reference teaching 2,4-dimethylphenyl N-(3-dimethylaminopropyl) carbamate), *In re MEHTA* 146 USPQ 284, (2-(1-methyl)-pyrrolidylmethyl benzilate obvious over a reference teaching 3-(1-methyl)-pyrrolidylmethyl benzilate), "[t]he fact that a **position isomer** (emphasis added) of a compound is known is some evidence of the obviousness of that compound. **Position isomerism** (emphasis added) is a fact of close *structural* (emphasis in original) similarity ...". *Deutsche Gold-Und Silber-Scheideanstalt Vormals Roessler v. Commissioner of Patents*, 148 USPQ 412, (1-azaphenothiazines obvious over references teaching 2-azaphenothiazines, 3-azaphenothiazines, and 4-azaphenothiazines), *In re Crounse*, 150 USPQ 554 (dye with *para* (CONH₂) and *ortho* (OCH₃) obvious over a dye with the same nucleus and *meta* (CONH₂) and *para* (OCH₃) group), *Ex parte Allais*, 152 USPQ 66, (3-β-aminopropyl-6-methoxyindole obvious over a reference teaching 3-β-aminopropyl-5-methoxyindole), *In re Wiechert* 152 USPQ 247, (1-methyl dihydrotestosterones obvious over a reference teaching 2-methyl dihydrotestosterones), *Monsanto Company v. Rohm and Haas Company*, 164 USPQ 556, at 559, (3',4'-dichloropropionanilide obvious over references teaching 2',4'-dichloropropionanilide and 2',5'-dichloropropionanilide), *Ex parte Naito and Nakagawa*, 168 USPQ 437, (3-phenyl-5-alkyl-isothiazole-4-carboxylic acid obvious over a reference teaching 5-phenyl-3-alkyl-isothiazole-4-carboxylic acid), "[t]his merely involves **position isomers** (emphasis added) and under the decisions cited, the examiner's holding of *prima facie*

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obviousness is warranted." *In re Fouche*, 169 USPQ 429, (10-aliphatic substituted derivatives of dibenzo[a,d]cycloheptadiene obvious over reference teaching 5-aliphatic substituted derivatives of dibenzo[a,d]cycloheptadiene). *In re Hass* 60 USPQ 552, which found a *prima facie* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ulliot*, 103 USPQ 185, which found a *prima facie* case of 2-oxo-quinolines obvious over prior art a 1-oxo-isoquinoline, *In re FINLEY*, 81 USPQ 383, 2-ethyl hexyl salicylate over octyl salicylate.

Ex parte Engelhardt, 208 USPQ 343 at 349, "[i]f functional groups capable of withdrawing or repelling electrons are located in the chain or **ring** (emphasis added) of a biologically active compound, transfer of such groups to other positions in which their electronic effects are lessened or enhanced may alter the biological activity of the modified compound. Hence, **position isomerism** (emphasis added) has been used as a tool to obtain new and useful drugs", *In re Grabiak* 226 USPQ 870, "[w]hen chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made", *In re Deuel* 34 USPQ2d 1210, "a known compound may suggest its analogs or isomers, either geometric isomers (*cis v. trans*) or **position isomers** (emphasis added) (*e.g. ortho v. para*)".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 7,176,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because the

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'215 patent claims a carbon atom that is substituted for the identity of Y. If this is substituent is a aminophenyl, position isomers of the instant case are created.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571) 272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.


RITA DESAI
PRIMARY EXAMINER

11/29/07

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